

Message

From: Bette Meek [bmeek@uottawa.ca]
Sent: 4/4/2021 5:19:20 PM
To: Calvin Willhite [Ex. 6 Personal Privacy (PP)]; Allan H. SMITH [ahsmith@berkeley.edu]; tsujij@exponent.com; Harvey Clewell [hclewell@ramboll.com]; Cohen, Samuel M [scohen@unmc.edu]; Shao, Kan [kshao@indiana.edu]; Michael [Ex. 6 Personal Privacy (PP)]; Lee, Janice [Lee.JaniceS@epa.gov]; Thayer, Kris [thayer.kris@epa.gov]; Orme-Zavaleta, Jennifer [Orme-Zavaleta.Jennifer@epa.gov]
Subject: RE: SOT Arsenic Symposium

Dear Calvin and All:

Really unfortunate - the tendency of articles, compiling a list of observed positive associations, without any attempt to meaningfully interpret the data in integrative mode of action context, taking into account whether available data support expected patterns of empirical support and essentiality of envisaged key events. While this is OK, I guess, in, perhaps identifying relevant data for more meaningful organization and assessment, unfortunately, it's never presented this way.

A clarification, also; there is one mode of action for substances inducing a specified adverse outcome, in this case, consistent with pathways described for fine particulate matter (PM2.5) inducing related effects on the c.v. and neurological systems. Key events in hypothesized modes of action represent nodes of convergence of mechanistic pathways and while several mechanistic pathways contribute to early key events, there is generally convergence at later stage to produce the adverse effect. Suggest that we avoid reference to the term "multiple modes of action" often erroneously referenced in relation to the same adverse effect.

Different adverse effects may well be associated with different causal pathways.

However, while I'm not up to speed on the latest data on arsenic, isn't it the consistency of effects at relatively low concentrations observed in epidemiological studies (with some support of biological plausibility) that's influential, here?

Best,

Bette

From: Calvin Willhite [mailto:Ex. 6 Personal Privacy (PP)]
Sent: April 3, 2021 3:50 PM
To: Allan H. SMITH <ahsmith@berkeley.edu>; Joyce Tsuji <tsujij@exponent.com>; Harvey Clewell <HCllewell@ramboll.com>; Cohen, Samuel M <scohen@unmc.edu>; Shao, Kan <kshao@indiana.edu>; Bette Meek <bmeek@uottawa.ca>; [Ex. 6 Personal Privacy (PP)]; Lee, Janice <Lee.JaniceS@epa.gov>; Thayer, Kris <thayer.kris@epa.gov>; Orme-Zavaleta, Jennifer <Orme-Zavaleta.Jennifer@epa.gov>
Subject: SOT Arsenic Symposium

Attention : courriel externe | external email

I don't know that I can endorse the attached human health observations on arsenic, but if true we can now add dementia to the long list of adverse health outcomes.

This comes as very bad news.

Dr. Tsuji will cover cardiovascular aspects of chronic arsenic intoxication. From the attached it appears there are multiple MOAs and multiple target organs in addition to its inhibition of sulfhydryl enzymes.

One focus of the proposed Symposium is not only the shape(s) of the low-dose aspects of arsenic of which there appear to be many, but also which of the

many different adverse outcomes should drive the As health risk assessment.

Hopefully Program Committee will see the importance of the problem.